

TECHNICAL MANUSCRIPT REVIEW FORM

Title "State-of-the-Science Report on Predictive Models and Modeling Approaches for Characterizing and Evaluating Exposure to Nanomaterials"		Author(s) EPA/ORD John M. Johnston RTI International Stephen M. Beaulieu Michael I. Lowry Evan Bowles
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Type of Publication/Audience Research		Reviewer/Organization/Address Dr. Sam Luoma UC Davis John Muir Institute of the Environment The Barn 122B University of California One Shields Avenue Davis, CA 95616-8527
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You are asked to review and comment on the attached manuscript. Feel free to make notations on the manuscript as well as in the comments section below, particularly regarding your recommendations for revisions. If you are unable to review the manuscript by the required date, please return it now. Your suggestions for alternate or additional reviewers will be welcomed.

SUMMARY RATING			RECOMMENDATIONS
Please rate the manuscript as follows:	Satisfactory	Unsatisfactory	<input type="checkbox"/> (1) Acceptable as is <input type="checkbox"/> (2) Acceptable after minor revisions <input type="checkbox"/> (3) Acceptable after major revisions <input type="checkbox"/> (4) Not acceptable If you have checked either 3 or 4, please specifically state reasons(s) in the comments space below. I can't judge this not knowing what the agency wanted. If an annotated compendium of literature satisfies the agency then the report is satisfactory. If management was hoping to learn something useful about how to proceed with models and nanomaterials then it is not acceptable for the reasons stated below and would require major revisions. Whether these authors are capable of the synthesis necessary to achieve this goal is an important question.
Content & scope	Narrow		
Organization & presentation	Satisfactory		
Quality of data & validity of analytical techniques	satisfactory		
Soundness of Conclusions	Too few		
Editorial Quality	satisfactory		
Other (specify): Quality of literature review	A description not a synthesis with ocnclusions		
Analysis of fate and transport	Satisfactory		
Analysis of bioavailability, bioaccumulation and biological aspects of exposure	Unsatisfactory		
			Reviewer's Signature Samuel Luoma Date 02/09/10

Comments: (Use extra sheets if needed):

This is an adequate description of the literature focused on fate and transport and as a compendium of selected literature it could be useful. Appendix B is an interesting systematic approach to evaluating the models presented.

But the report is not a synthesis of the literature. With a few exceptions there are few conclusions drawn from which management could take direction or researchers can learn. Section 2 is essentially a review of a few reviews; not a review of the primary literature. Section 4 is a useful compendium of modeling approaches. But the approaches are described not discussed, in almost all cases. . With one exception there is no synthetic analysis comparing the approaches: how different approaches are similar, how they are different, what their strengths are and what their limits are and what all that means for moving forward with modeling. The authors have worked hard gathering the literature; there is no evidence they have thought carefully about what it means as a whole.

The failure to differentiate among classes of NM is a major flaw in the report. At least a breakdown between carbon based and metal-based NM would have been useful because the modeling approaches for the two will be different, based upon what we know about their chemical analogues (and many but not all of those differences will apply to NMs).

A paper on modeling should include individual conceptual models to start every subject (where "subject" is defined by the elements in the overall conceptual model in Figure 1-2). That might help bring out some conclusions, which the report is sorely lacking. One big conclusion that strikes me is that the scientific models published to date on fate and transport (described in section 4) are all sub-models of a specific process. The authors could discuss why is the case and whether the development of such models might be a valid approach to building more comprehensive and integrated models. The literature is much more rich in ideas than presented here about how to approach the challenge of a small knowledge-base and growing demand for regulation. Is one of the authors' implied conclusions that there is not enough understanding to build informed models, but because we need models to make decisions we should go ahead anyway? Aren't there disadvantages to this – i.e. mis-leading models that lead to wrong decisions? Do we really need models to make decisions? Is a systematic research agenda required to populate the models? What is that agenda and what does the literature say should be the elements of that agenda? Many documents have addressed the latter question. The authors describe some of those but the conclusions are not brought forward.

Bioavailability and bioaccumulation are key processes in determining exposure. The description of this literature and the review are wholly inadequate. They do not include many important concepts. They are taken from dated concepts and literature focused on organic chemicals. The metals literature is totally absent; but yet many of the NMs are metal-based. There certainly are more and better approaches available than those described here. It is not clear the authors have the capability to address this subject. I suggest the report be restricted to fate and transport; and the existing sections on bioaccumulation be deleted as mis-leading.

As much as 20% of the report describes how the literature review was done. This is superfluous filler material that takes away from the credibility of the document. If the authors want to prove that how much effort they put in, then this at the most should go in an appendix. Lists of important scientists and important laboratories are also not valuable and are destined to raise hackles. These lists make it clear the authors are not appreciative of the international effort currently underway in this field. Many people who are leaders in this field are not included (e.g. Greg Lowry, even though he is cited is not on the list; Simon Apte, Jamie Lead, etc.). Why upset them with such lists. It leaves the perception the authors have nothing thoughtful to say themselves. Finally, the executive summary is a list of activities conducted to create the report. Readers are not interested in what the authors had to do; they want to read what the authors learned and concluded.

The choice of literature is selective not comprehensive. Perhaps this was the charge? Important reviews relevant to exposure have been authored by Owen and Handy, Colvin, Maynard and Luoma among many others. These are not considered or even listed in the literature cited. The list is also quite parochial; with USEPA insiders dominant. For example, the British Royal Society and the Royal Commission on Environmental Pollution have published important multi-authored documents that are insightful and would be useful as a guide for future directions. There has been an emphasis by agencies (including EPA) to seek and internationally cooperative effort in advancing our understanding of the environmental implications of nanotechnology. The report gives inadequate sense of this either in its citations or its content.

Sam Luoma comments provided 9/2/10

1. Is the report written in a clear, concise, and readable manner? If not, please provide comments. Yes
2. Do the issues identified adequately address the breadth of potential fate, transport and modeling issues related to multimedia modeling of nanomaterials in soil and water media? To some degree. Areas like bioaccumulation are poorly done.
3. Are there additional studies or other information that should be included in this report? If so, please cite or identify that information. A whole literature on bioaccumulation is missing.
4. Do the identified research needs adequately address knowledge gaps about multimedia modeling of nanomaterials in soil and water media? Please identify any additional research gaps that you think should be identified. No. this is the major deficiency of the report. There is little synthesis, few useful conclusions and no direct statement about specifically what is needed to move forward in this arena.
5. Are you aware of critical literature references not included, but should have been included in the bibliography? If so, please list them. Many. But I think it is the authors' job to fill in the gaps I have identified.